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Three-year experience of a dedicated prostate mpMRI pre-biopsy programme and effect on timed cancer diagnostic pathways

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AIM: To evaluate the effect of pre-biopsy magnetic resonance imaging (MRI) on cancer diagnostic times, and to report MRI-directed pathology outcomes.

MATERIALS AND METHODS: In total, 1483 patients were referred with prostate cancer suspicion during a 30-month period. Upfront MRI was performed in 745 patients: 332 MRIs in the 15 months prior to dedicated scanning slots (group 1), and 413 in the 15 months post-introduction (group 2). A further 88 patients had initial MRI following clinical assessment. Biopsy via the transrectal (TR) or transperineal (TP) approach was performed, with MRI/ultrasound fusion for MRI targets. Clinically significant cancer (csPCa) was defined as Gleason ≥3+4. Negative MRIs were defined as Likert 1–2. Per-case clinical decisions were taken to biopsy or not.

RESULTS: 44.4% of patients avoided biopsy. 484/833 (58.1%) MRIs were negative; 37.4% of these patients had biopsy with a negative predictive value (NPV) of 92.8% for Gleason ≥3+4 and 98.3% for ≥4+3. Overall prostate cancer prevalence was 34.3% (24.6% csPCa). In 323 MRI-positive cases, any cancer was present in 78.9% (csPCa 60.4%). Of the 1483 patients, 1232 (83.1%) completed all diagnostic tests within 28 days. Upfront MRI patients met this standard in 621/833 (74.5%), improving from 66.9% to 81.1% with reserved slots (group 2) with a reduced diagnostic time from median 25.5 to 20.9 days. Biopsy scheduling delayed the pathway in

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69.7%, with MRI responsible in 22.3%, reducing to 10.3% in group 2. TP biopsies met the 28-day standard in significantly less cases (29.7%), compared to TR (67.4%, $p<0.0001$).

CONCLUSION: Reserved MRI slots reduces time-to-diagnosis, and upfront MRI safely avoids biopsy in a significant proportion of men, whilst maintaining expected csPCa detection rates.

Introduction

Prostate cancer is the leading cause of male cancer in the UK, with the mortality rate of the disease in the UK now exceeding that of breast cancer.[1] Level 1a evidence from several recent studies suggests that initial prostate magnetic resonance imaging (MRI) prior to biopsy can improve outcomes and potentially avoid unnecessary biopsy in selected patients.[2–6]

Within the UK system, referral to a specialist for investigation of suspected cancer is time monitored at various stages of the pathway. Recent recommendations include the introduction of a new 28-day diagnostic waiting target to replace the existing 14-day standard, wherein 50% of patients should have cancer definitively diagnosed or excluded within 14 days and 95% within 28 days.[7]

Current UK guidelines only recommend pre-biopsy multiparametric MRI in patients with a history of negative biopsy and persistent suspicion of prostate cancer.[8] Nevertheless, up to 73% of NHS trusts in England already offer MRI to biopsy naive men.[9,10] Prostate MRI pre-biopsy may be a potential means of improving cancer targets, in particular, if some biopsies can be avoided. However, in patients where biopsy is still required, the diagnostic work-up can be challenging, requiring resource-limited MRI examinations to be scheduled and reported, a biopsy, which may require theatre time, and typically >12 biopsy cores to be reported by pathologists. Contemporary UK cancer referral data suggest that the median diagnostic interval for all cancer patients is 40 days; however, for prostate cancer, the median time to diagnosis increases to 55.5 days, highlighting these challenges.[11]

An "upfront" MRI service was implemented at Addenbrooke's Hospital for prostate cancer diagnosis in October 2015, which subsequently included a set number of reserved MRI time slots, 15 months into the process. The aim of the present study was (1) to evaluate the effect of this new pathway on cancer diagnostic waiting times and (2) to compare outcomes against contemporary MRI pre-biopsy studies.

Materials and methods

This retrospective analysis of a prospectively maintained database was part of a service evaluation of the prostate diagnostic pathway, with the need for informed consent for data analysis waived by the Local Ethics Committee. The study was performed in accordance with the Declaration of Helsinki. Data were evaluated from all patients presenting to the prostate diagnostic clinic (PDC) during a 30-month period (1/10/2015 to 31/3/18), following the introduction of a formal MRI pre-biopsy programme.

Patients qualified for fast-track "upfront" MRI prior to the clinic appointment following telephone assessment by a member of the urology team and when meeting the following criteria: no clinical contraindication to MRI, prostate specific antigen (PSA) value of ≤30 ng/ml, life expectancy ≥10 years, and fitness for radical therapy (for those ≥71 years, an assessment in clinic was required), and exclusion of infective symptoms.

MRI parameters

Patients underwent prostate MRI using a 1.5 T MR450 or a 3 T HDx Discovery MR750 HDx system (GE Healthcare, Waukesha, WI, USA) with a 16–32 channel phased-array coil. Unless contraindicated, intravenous injection of hyoscine butylbromide (Buscopan, 20 mg/mL, Boehringer, Germany) was administered prior to imaging to reduce peristaltic movement. Axial T1-weighted fast spin echo (FSE) pelvis, and T2-weighted FSE prostate (axial/sagittal/coronal) images were acquired. Axial T2-weighted: 85 ms echo time (TE)/3,700–5,000 ms repetition time (TR); 24×24 cm field-of-view (FOV); 256×256 matrix; 3–3.5 mm section thickness; 0–0.5 mm gap. Diffusion-weighted imaging (DWI) was performed using a spin-echo echo-planar imaging pulse sequence 60 ms TE/3,000–3,400 ms TR; 256×256 matrix; 3–4 mm section thickness; 0 mm gap, parallel imaging factor=2, signal averages=3/8 for 1.5/3 T with b-values of 150, 750, 1,000, and 1,400 s/mm^2; with additional b=2,000 s/mm^2 at 3 T. Apparent diffusion coefficient (ADC) maps were calculated automatically. Dynamic contrast-enhanced (DCE-)MRI axial three-dimensional (3D)-fast spoiled gradient-echo (FSPGR) was acquired (4,088 TR/1.788 ms TE, 24×24 cm FOV) following a bolus injection of gadobutrol (Gadovist, Bayer Healthcare) via a power injector, at a rate of 3 ml/s (dose 0.1 mmol/kg), temporal resolution 7/10 seconds at 3/1.5 T.

Image analysis

The MRI images were interpreted by one of three experienced uroradiologists. MRI sequences were evaluated based on the Prostate Imaging-Reporting and Data System (PI-RADS) structured scoring criteria, initially developed by the European Society for Urological Research (ESUR),[12,13] with weighting applied for T2-weighted and DWI scoring depending on peripheral zone (PZ) or transition zone (TZ) location. An overall impression was then used to derive a

Likert suspicion score, wherein Likert 1= clinically significant prostate cancer (csPCa) highly unlikely, 2= csPCa unlikely, 3= indeterminate for csPCa, 4= csPCa likely, 5= csPCa highly likely.[14]

Biopsy technique

Depending on clinical recommendation, biopsy was performed by either transrectal or transperineal approaches, using MRI/ultrasound fusion. All biopsy procedures were performed by experienced urologists and included systematic cores. In cases where targeted biopsy was additionally performed, at least two biopsy cores were taken from each lesion before systematic biopsies. Transrectal biopsy was performed using an office-based fusion platform (UroNav; InVivo Corp., Gainesville, FL, USA), with 12 systematic cores obtained. Transperineal biopsy was performed under general anaesthesia using the Biopsee fusion platform (Medcom, Darmstadt, Germany) with 24 systematic cores acquired according to the Ginsburg protocol.[15] Targets were defined as any Likert score 3–5 lesion on MRI. All targets were defined by radiologists pre-procedure using T2-weighted imaging as the primary and DWI as the secondary source images, using the DynaCAD system (InVivo Corp.) for transrectal and Biopsee software for transperineal approaches.

For negative MRI examinations, a case-by-case clinical decision was taken to biopsy or not following discussion with the patient and clinical risk assessment based on family history, absolute PSA $<$10 ng/ml, and PSA density $\leq$0.1 ng/ml/cm^3. Patients with a negative MRI and no biopsy were followed up for a minimum of 6 months and had at least one subsequent PSA reading.

Histopathology

All biopsies were graded with Gleason scores according to the International Society of Urological Pathology (ISUP) 2005 recommendations[16] by a uropathologist and reviewed by another uropathologist within the setting of a multidisciplinary team (MDT) meeting. The final histology result following this assessment was used as outcome data for the study.

Pathway assessment

The proposed NHS 28-day diagnostic standard was applied post hoc to the patient pathways and divided into clinic patients undergoing MRI pre-biopsy and those undergoing other initial investigations. The first group was further divided into pathway patients presenting in the 15 months prior to (1/10/15–31/12/16) and 15-month period after (1/1/17–31/3/18) the introduction of reserved MRI slots. For MRI patients, the pathway was subdivided into the time components of final MRI report availability (from time of clinic referral), biopsy being performed (from time of MRI report), and time to report biopsy (from time of biopsy completion). For purposes of meeting the 28-day standard, it was assumed that each of the three components should be performed in $\leq$9 days to avoid delaying the pathway.

Statistics

The Shapiro–Wilk test assessed the distribution of age and PSA with intergroup comparison performed using the Mann–Whitney *U*-test. An intergroup comparison of median times to schedule and report MRI and biopsy, and to reach the 28-day target, was conducted using the Mann–Whitney *U*-test. Pearson's chi-square test was used to assess the relationship between groups meeting the 28-day target, and for the effect of biopsy type on meeting the target. Spearman's rank correlation test was used to assess correlation between the duration of each diagnostic procedure and meeting the target.

Results

During the 30-month period, 1,483 patients were referred to the prostate cancer diagnostic clinic (PDC) with suspicion of prostate cancer (Fig 1); of those, 745 patients (53%) met the criteria for MRI prior to the clinic visit. Of the remaining 738 patients, 88 also proceeded to MRI after initial consultation. Thus 833/1,483 (56.2%) PDC patients had MRI as their first investigation, of which 710 (85.2%) were performed at 3 T and at 123 (14.8%) at 1.5 T. Patients undergoing MRI first had a significantly lower mean age of 62.4 years (median 63, IQR 58–67 years) and lower PSA 8 ng/ml (median 6, IQR 4.6–8.9 ng/ml) compared to non-MRI patients at 75 years (median 75, IQR 70–81 years) and 27.3 ng/ml (median 10, IQR 6.3–18.1 ng/ml), respectively (both $p<0.0001$).

Upfront MRI outcomes

484 of 833 patients (58.1%) were reported as MRI negative (Likert score 1–2). Of these, 140/484 (28.9%) proceeded directly to biopsy based on clinical risk assessment and patient discussion. 108 of the 140 biopsies were benign (77.1%), 21 showed Gleason 3+3 disease (15%), eight showed Gleason 3+4 (5.7%), two showed Gleason 4+3 (1.4%), and one showed Gleason 4+4 (0.7%) disease (Table 1). On retrospective review, the Gleason 4+4 tumour was visible at the low apex and one Gleason 3+4 lesion was identified as a 4×2 mm left base focus. A further 41 patients underwent biopsy during the follow-up period at a mean time of 10.2 months (median 9, range 2–25 months). 26 of the 41 of these biopsies were benign (63.4%), 13 showed Gleason 3+3 disease (31.7%) and two showed Gleason 3+4 disease (4.9%). The remaining 303 patients with no biopsy were followed up clinically for an average 20.7 months (median 19, range 6–19 months). Thus, a total of 181 patients with a negative MRI had an immediate or subsequent biopsy, with 134/181 (74%) benign; MRI having a negative predictive value (NPV) of 92.8% for Gleason $\geq$3+4 and 98.3% for $\geq$4+3 disease.

An MRI lesion was reported in 349 patients. 79 of 103 patients (76.7%) with Likert score 3 underwent targeted biopsy, of these 50.6% were benign, and 15/79 (19%) showed Gleason $\geq$3+4 disease. All 83 patients with Likert 4 findings

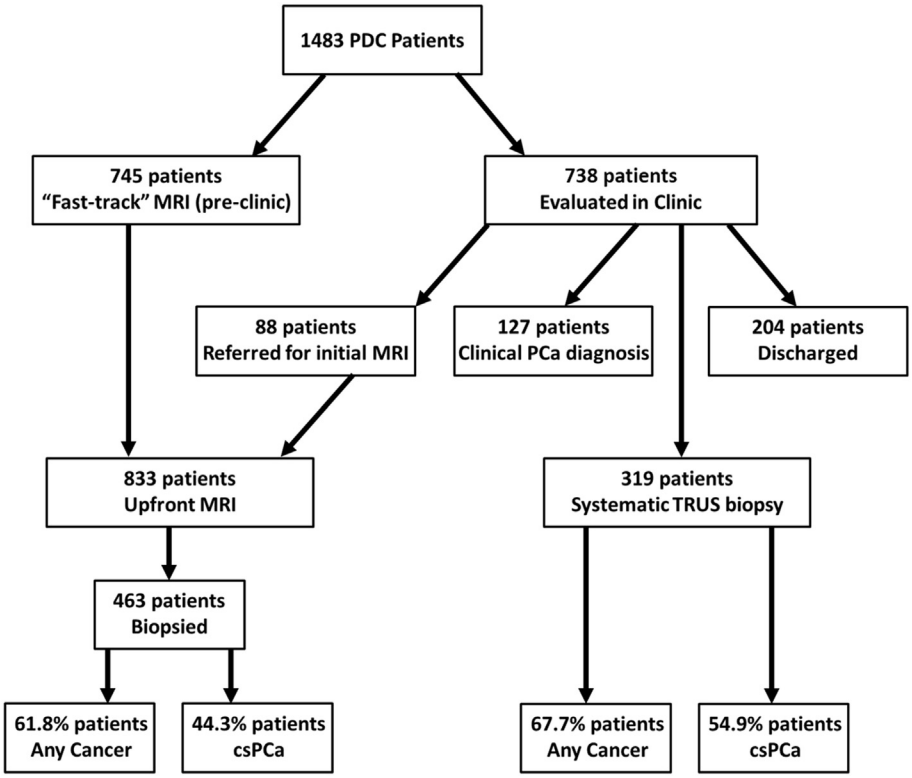

Figure 1 Study flowchart for all men presenting to the prostate diagnostic clinic (PDC). TRUS = transrectal ultrasound; csPCa = clinically significant prostate cancer.

underwent biopsy, with 73.5% showing any cancer and 49.4% Gleason ≥3+4. Of the 163 Likert 5 MRI lesions, 161 were biopsied, with 96.3% showing any cancer and 139/161 (86.3%) having Gleason ≥3+4 disease. For combined MRI-positive cases (Likert score 3–5), 68/323 were benign (21.1%), 60 (18.6%) had Gleason 3+3, and 195 (60.4%) Gleason ≥3+4 disease (Fig 2). In the cohort of 833 MRI patients, 286 had prostate cancer (34.3%), of which 205 (24.6%) were Gleason ≥3+4 (Table 2). In total 463/833 (55.6%) patients undergoing initial MRI were biopsied, with 370 (44.4%) avoiding biopsy.

Other PDC outcomes

Six hundred and fifty of 1,483 PDC patients (43.8%) did not receive MRI as their first investigation. The most frequent initial management step was systematic TR ultrasound biopsy in 319 (49.1%) patients, bone scintigraphy, or CT for immediate staging in 127 (19.5%) patients, or discharge with treatment deemed unnecessary or unsuitable in 114 (17.5%) patients (Table 3). Of the 319 patients undergoing biopsy, results were benign in 103 (32.3%), Gleason 3+3 in 41 (12.9%) and Gleason ≥3+4 in 175 (54.9%) patients. Twenty-nine of the 114 biopsy-negative cases (25.4%) proceeded to MRI due to ongoing clinical suspicion, at a mean time of 5.2 months after initial biopsy (median 4, range 2–19 months). Targeted biopsy was performed in 18 of these 29 cases (62.1%), 16/18 of which showed cancer: Gleason 3+3 five, 3+4 in seven, 3+5 in one, and 4+3 in three patients.

Twenty-eight-day diagnostic standard

Of the 1,483 patients, 1,232 (83.1%) patients completed all diagnostic tests with results available within the 28-day standard. Patients receiving MRI as the first investigation only met the standard in 621/833 cases overall (74.5%; Table 4). A significantly higher percentage of patients assessed in clinic and not preceding to MRI met the standard: 611/650 (94%). These patients had a lower median of

Table 1
Magnetic resonance imaging outcomes by Likert score.

MRI Score	Total (%)	Biopsied (%)	Benign (%)	Any cancer (%)	GS ≥3+4 (%)
Likert 1/2	484 (58.1)	140 (28.9)	108 (77.1)	32 (22.9)	11 (7.9)
Likert 3	103 (12.4)	79 (76.7)	40 (50.6)	39 (49.4)	15 (19)
Likert 4	83 (10)	83 (100)	22 (26.5)	61 (73.5)	41 (49.4)
Likert 5	163 (19.6)	161 (98.8)	6 (3.7)	155 (96.3)	139 (86.3)
Total	833/833 (100)	463/833 (56.3)	177/463 (38.2)	286/463 (61.8)	205/463 (44.3)

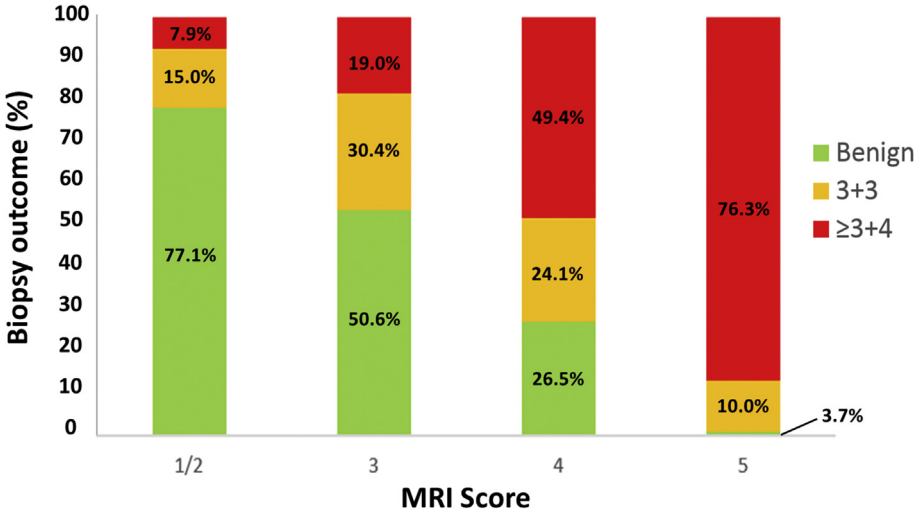

Figure 2 Proportion of men Gleason 3+3 (insignificant), Gleason 3+4 (clinically significant) cancer, or benign findings on MRI by MRI score.

15 days (IQR 9–21 days) for pathway completion compared to 22 days for MRI-first patients (IQR 14–30 days), with the rate of meeting the target significantly higher (OR= 3.8, 95% CI: 2.86–5.16; $p<0.001$).

332 patients underwent upfront MRI in the first 15 months prior to reserved slots (group 1), and 413 had MRI in the 15 months post-introduction (group 2; Electronic Supplementary Material Table S1). The biopsy rate was identical between the two groups at 55.7%: 185/332 and 230/413, respectively.

There was no significant difference in mean age (p=0.991) or PSA (p=0.441) between group 1 at 62.4 years (median 64, IQR 59–67 years) and 8.3 ng/ml (median 6, IQR 4.5–8.9 ng/ml), respectively, and group 2 at 62.4 years (median 63, IQR 58–67 years) and 7.7 ng/ml (median 6, IQR 4.7–8.9 ng/ml), respectively. There was a significant reduction in time to scheduled MRI from an average of 8.99 days (median 9, IQR 6–12 days) to group 2 at 5.29 days (median 5, IQR 3–7 days), but with similar times to report at a mean of 1.98 and 1.76 days, respectively (Table 5).

Group 1 (MRI without reserved appointment slots)

Of the 332 patients on this pathway, 222 (66.9%) patients completed all diagnostic investigations within 28 days. Of the 110 cases not meeting the standard, scheduling of biopsy was primarily responsible in 64 cases (58.2%), MRI in 34 (30.9%), and time to report biopsy in 12 cases (10.9%). All 3 of MRI and biopsy scheduling/reporting took ≥9 days in 22/110 cases, two days in 34, and only one day component in 12 cases; Table 6. 176 of 332 (53.0%) MRIs were performed and reported within 9 days. Of the 185 cases undergoing biopsy, 82 (44.3%) were scheduled and performed within 9 days, and 142 (76.7%) of biopsies were reported within 9 days.

Group 2 (MRI with reserved appointment slots)

A significantly higher proportion of patients 335/413 (81.1%) completed investigations within 28 days, with the rate of meeting the target for group 2 patients significantly higher than group 1 (OR= 2.1, 95% CI: 1.49–2.85; $p<0.001$).

Table 2
Gleason grade of tumours.

Gleason	*n*	% of Cancer	% of biopsied	% of cohort
3+3	81	28.3	17.5	9.7
3+4	120	42	25.9	14.4
3+5	6	2.1	1.3	0.7
4+3	39	13.6	8.4	4.7
4+4	8	2.8	1.7	1
4+5	18	6.3	3.9	2.2
5+3	1	0.3	0.2	0.1
5+4	11	3.8	2.4	1.3
5+5	2	0.7	0.4	0.2
Total	286	100	61.8	34.3

Table 3
Management outcomes for non-magnetic resonance imaging prostate diagnostic clinic patients.

Outcome	*n*	%
Bone scintigraphy or computed tomography	127	19.5
Clinically benign	11	1.7
Not for treatment	114	17.5
Patient declined	10	1.5
Infective	10	1.5
PSA follow-up	59	9.1
Biopsied	319	49.1
Histopathology		
Benign	103	32.3
3+3	41	12.9
3+4	41	12.9
3+5	11	3.4
4+3	42	13.2
4+4	11	3.4
4+5	44	13.8
5+3	1	0.3
5+4	18	5.6
5+5	7	2.2

PSA, prostate specific antigen.

Table 4
Patient pathways compared to 28-day standard.

Cohort	Total (*n*)	Missed (*n*)	% Met
Non MRI pathway	650	39	94
Non MRI pathway (MRI 1st)	88	24	72.7
Upfront MRI (non-reserved)	332	110	66.9
Upfront MRI (reserved)	413	78	81.1
All MRI first	833	621	74.5
All	1483	251	83.1

MRI, magnetic resonance imaging.

Numbers meeting the 28-day standard were also significantly higher for the subset of patients undergoing biopsy with 63.0% in group 2 and 43.2% in group 1 (OR= 2.2, 95% CI: 1.51–3.33; $p<0.001$). Of the 78 cases not meeting the standard, scheduling was primarily responsible in 67 cases (85.9%), MRI in 8 (10.3%) and biopsy reporting in 3 cases (3.8%). All three components took >9 days in 43/78 cases, two components in 33 cases, and only one component in two cases; 357 of 413 (86.4%) MRI examinations were performed and reported within 9 days. Of the 230 cases undergoing biopsy, 98 (42.6%) were scheduled and performed with 9 days, and 208 (90.0%) were reported within 9 days.

Type of biopsy

TR biopsy was performed in 270/415 (65.2%) and transperineal (TP) in 145/415 (34.8%) of cases. Patients undergoing TR biopsy met the 28-day standard in 182/270 (67.4%), significantly higher than TP in 43/145 (29.7%). TP biopsy had a higher overall mean number of days to complete investigations at 35.4 days (median 34, IQR 28–41 days) compared to TR at 26.7 days (median 25, IQR 21–31 days). The rate of meeting the target for patients with TR biopsy was significantly higher (OR= 5, 95% CI: 3.20–7.70; $p<0.001$). On average, TP took significantly longer to schedule at 18.5 days (median 16, IQR 12–25 days) and to report biopsies at 8.6 days (median 8, IQR 6–11 days) compared to TR at 11.5 (median 10, IQR 7–14 days) and 6.6 days (median 6, IQR 5–8 days), respectively (both $p<0.0001$).

Discussion

The present study investigates the outcomes of a dedicated upfront prostate MRI programme in biopsy-naive men and the effect this has on timed cancer pathways. This large standard clinical care cohort comprised all men referred for MRI, including those with pelvic metalwork and artefact or technical issues affecting image quality. The present results show comparable outcomes to contemporary prospective MRI pre-biopsy studies[2–6] and enabled overall biopsy avoidance in 44%. Streamlining MRI referrals improved the number meeting the 28-day diagnostic standard from 66% to 81%. Although significantly below the retrospectively applied target of 95%, this has to be balanced against the advantage of getting it right first time, potentially saving additional patient anxiety and healthcare costs.

Overall 83.3% of the 1,483 patients achieved the 28-day standard, with the highest number (94%) being within the non-MRI cohort. This is likely explained by a proportion of patients being deemed clinically benign/inflammatory or inappropriate for treatment, and thus, immediately discharged, or from being clinically diagnosed with prostate cancer based on raised PSA and proceeding directly to staging investigations (Table 1). The latter also likely explains the significantly higher PSA level within this group; an older mean age is also expected given the selection criteria for upfront MRI including fitness for radical therapy and life expectancy of ≥10 years.

In the group with reserved MRI slots, the medium time to completion of diagnostic tests was 20.86 days (IQR 12–28), which is significantly lower than the recently reported 55.5 days (IQR 29–126) UK average for prostate cancer.[11] MRI was responsible for delays to the pathway in 30.9% of the

Table 5
Time taken for each component of the diagnostic pathway.

	Schedule MRI	Report MRI	Schedule biopsy	Report biopsy	Completed pathway
Combined	6.94 (4–9)	1.86 (1–3)	13.92 (7–17)	7.27 (5–9)	22.91 (14–29)
Group 1	8.99 (6–12)	1.98 (1–3)	13.69 (7–17)	7.96 (6–10)	25.45 (15–32)
Group 2	5.29 (3–7)	1.76 (1–3)	14.1 (8–17)	6.71 (5–8)	20.86 (12–28)
Group 1 versus 2 (*p*-value)	<0.0001[a]	0.123	0.662	0.006[a]	<0.0001[a]

[a]$p<0.05$.

Table 6
Component of pathway responsible for missing 28-day target.

	All		Non-reserved MRI slots		Reserved MRI slots		*p*-Value
	Total missing	Primarily responsible (*n*=188)	Total missing	Primarily responsible (*n*=110)	Total missing	Primarily responsible (*n*=78)	
MRI (+report)	524/745 (70.3%)	42 (22.3%)	167/332 (53%)	34/110 (30.9%)	357/413 (86.4%)	8/78 (10.3%)	<0.001[a]
Scheduling biopsy	180/415 (43.3%)	131 (69.7%)	82/185 (44.3%)	64/110 (58.2%)	98/230 (42.6%)	67/78 (85.9%)	0.802
Report biopsy	350/415 (84.3%)	15 (8%)	142/185 (76.7%)	12/110 (10.9%)	208/230 (90%)	3/78 (3.8%)	<0.001[a]

[a]$p<0.05$.
MRI, magnetic resonance imaging.

present cohort prior to the introduction of reserved slots, but only 10.3% after. In both cases, scheduling of biopsy caused the longest delay, failing to meet the nominal 9-day mini target in 43.1% of patients across the groups. Despite this, a reduction in overall pathway time between the groups was driven by an increased proportion of MRI examinations being completed in ≤9 days in group 2 (86.4% versus 53%) and additionally by lower biopsy reporting time (90% in group 2 were completed in 9 days). Previous authors have shown upfront MRI can reduce diagnostic times from 6 to 4 months, driven by providing an earlier definitive diagnosis for MRI-negative patients and getting it right first time.[17] There is a risk that meeting the 28-day diagnostic standard over-relies on a high proportion of negative MRI examinations; however, as an identical proportion of men (55.7%) underwent biopsy in groups 1 and 2, this was therefore not a confounding factor for inter-group comparisons.

TP biopsy took significantly longer to schedule at 18.5 compared to 11.5 days for TR and for biopsy reporting (8.6 versus 6.6 days), with only 29.7% of patients undergoing TP biopsy completing the pathway in 28 days compared to 67.4% for TR biopsy. This is expected given the necessity for a general anaesthetic and scheduling of theatre time, and the increased number of cores acquired, resulting in additional pathology workload. A move towards local anaesthetic technique for TP biopsy and with fewer cores may help limit scheduling delays.[18] It may also be possible to create more time in the pathway for scheduling of biopsies by aiming to complete MRI and reporting in 7 days and implementing a recommended pathology turnaround time of 5 days.[19] Another potential solution is a “one-stop” approach to biopsy,[20] which also mitigates against patients cancelling subsequent biopsy appointments; however, this may not be appropriate in all cases, particularly if theatre time is required, or if the decision to biopsy is less definitive (Likert 3 or negative MRI with borderline clinical risk factors), and the timeline may be insufficient to allow fully informed consent in such instances.

There have been four recent prospective trials assessing MRI for prostate cancer work-up, providing Level 1 evidence for its benefit in detection of csPCa and potential to avoid biopsy in cases of low suspicion.[2,3,5,6] The costs of an MRI-led diagnostic service are estimated to be 14.6% higher than traditional TRUS biopsy pathways[17]; however, this assumes all men receive a biopsy procedure and avoiding this in a subset of men will likely overcome this differential, and may even lead to cost savings.[21] The present upfront MRI cohort of 833 patients shows comparable outcomes, with 34.3% patients having prostate cancer and 24.6% csPCa, which compares to 39.4% and 254%, respectively in the recent 4M study.[6] Previous prospective biopsy-naive studies reported a higher prevalence of csPCa at 32–39%,[2,3,5] this may in part reflect less restrictive inclusion criteria than the present cohort, which incorporated an upper PSA limit of 30 ng/ml. 58.1% of MRI examinations were reported as negative, which is significantly higher than earlier studies[2,3,5]; however, these studies were multi-site studies, with patients predominantly scanned at 1.5 T, which may limit the quality of MRI, whereas the more comparable single-centre 3 T 4M study had a similar rate of 49%, and the single-centre BICOD biparametric study additionally reported a higher negative MRI rate at 37%.[4,6] Even allowing for subtle differences between the Likert and PI-RADS scoring systems, the present overall csPCa cancer detection rates for positive MRI were also comparable to these studies with Likert score 3 being 19% (versus 12–21%), 4 at 49% (32–60%) and score 5 at 86% (69–83%; Electronic Supplementary Material Table S2). The designation of an indeterminate MRI score of 3 in 12% of patients was lower than earlier studies that reported a rate of 21–29%, but again closer to the 6% rate in the single centre 4M study.[2–6] 44.4% of the present cohort avoided biopsy, higher than the theoretical 27% and 28% of the PROMIS and PRECISION studies, but more equivalent to the proposed 49% in the 4M study, and the risk stratified suggestion of 41% in the BICOD study.[2–6] The overall excess detection of clinically insignificant Gleason 3+3 cancer in the cohort was low at 9.7%, and equivalent to other target biopsy study cohorts with rates of 8.6–14.1%.[3,6,22] This low rate was achieved despite incorporating systematic background cores in all cases and including data from negative MRI cases that were biopsied, with the low number likely reflecting the avoidance of biopsy in the majority of MRI-negative cases.

The present study has some limitations including its single-centre experience and the retrospective nature of analysis. The results may not be repeatable in all centres and it should be noted that the quality of MRI acquisition and reporting should be ensured and audited before MRI is used as a means to avoid biopsy.[23] The true negative rate cannot be fully established in men not undergoing biopsy, and there is potential for sampling error leading to a false-negative result in cases of both a negative or positive MRI; however, all men underwent a minimum of 6 months of clinical follow-up (mean 20.7 months), with at least one repeat PSA. Reassuringly, the NPV of MRI for the 37.3% of negative MRI patients biopsied was high at 92.8% for Gleason ≥3+4 and 98.3% for ≥4+3, despite these men being selected for biopsy due to being at higher clinical risk based on PSA, PSA density or velocity, and/or family history. The definition of csPCa is not universally agreed, with some suggesting a higher threshold of Gleason ≥4+3 should apply, and others arguing that high-volume Gleason 3+3 can also constitute significant cancer.[24,25] A proportion of men with Likert 3 MRI examinations did not undergo biopsy based on clinical assessment, MDT discussion, and/or patient choice. The detection rate of csPCa in Likert 3 scores was low at 19%, justifying this approach, and was consistent with prior studies with similar csPCa detection rates of 12–21%.[2,3,5,6] Further iterations of prostate guidelines may help to subdivide indeterminate lesions to decide which require biopsy.[26,27] The 28-day diagnostic standard was applied post hoc in a retrospective manner and was not a prospective requirement during the time of the study thus,

with addition of dedicated resources, improved results may be possible. Furthermore, the applied standard of 9-days for each component of the pathway and that every component be allotted equal time is somewhat arbitrary, for instance NHS England suggests only a 5-day standard for pathology reporting.[19] it should also be noted that even the more aggressive forms of prostate cancer are relatively indolent compared to other tumour types and that evidence for a benefit for diagnosis within 28 days or treatment within 62 is lacking,[28] for instance, there is no overall survival benefit incurred with prostatectomy performed in 0–3 versus 4–6 months of diagnosis.[29]

In conclusion, a dedicated upfront MRI programme can safely avoid biopsy in a significant proportion of men, whilst maintaining expected detection rates for clinically significant prostate cancer. This has to be balanced against an increased time to diagnosis due to the challenging requirements of the diagnostic pathway; however, this can be partially mitigated through a protocol-driven rapid access referral with utilisation of reserved MRI slots.

Conflict of interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

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